Global views

The antibiotic susceptibility of *Neisseria gonorrhoeae* isolated in Ulaanbaatar, Mongolia

Introduction

The incidence and prevalence of gonorrhoea in Mongolia appear to be high and increasing.[1] Progress towards control of gonorrhoea requires the availability of effective antibiotic treatment. However, the susceptibility of *Neisseria gonorrhoeae* isolated in Mongolia is difficult to ascertain. A brief report some years ago noted "substantial" resistance to penicillins and quinolones and, surprisingly, third generation cephalosporins.[2]

Other factors decrease antibiotic availability. Some efficacious antibiotics recommended for treatment of gonorrhoea in developed countries are too expensive in Mongolia[1] so that tetracyclines, gentamicin, and quinolones are most often used. Antibiotics are also freely available from pharmacies in Mongolia, and treatments obtained from these sources may be multidose and uncontrolled. There is thus the potential for the development of further antibiotic resistance.

The susceptibility of gonococcal isolates from Ulaanbaatar to a number of antibiotics recommended for treatment in WHO standard guidelines and the in vitro susceptibility of gonococci to gentamicin, an aminoglycoside antibiotic currently used in Mongolia, is reported. Analysis of patterns of antibiotic resistance was enhanced by phenotyping gonococcal isolates.

Materials and methods

Fifty six unselected isolates from symptomatic patients (26 males and 30 females) attending the central STD clinic in Ulaanbaatar were identified by standard procedures. The minimum inhibitory concentration (MIC) and categorisation of the susceptibility of the isolates to penicillin, ciprofloxacin, spectinomycin, and ceftriaxone were determined by the standardised techniques.[3 4] High level tetracycline resistance (TRNG, MIC ⩾16 mg/l) and gentamicin susceptibility were determined by the same procedures. Chromosomal resistance to penicillin was defined as MICs ⩾1 mg/l and quinolone resistance when MICs were ⩾0.06 mg/l. Quinolone resistant strains were further divided into a "less susceptible" (MIC 0.06–0.5 mg/l) or "resistant" (MICs ⩾1 mg/l) group on the basis of ciprofloxacin MICs. β Lactamase production was determined by acidometric methods. Control cultures were WHO reference strains.

The gonococci were phenotyped by determining their auxotype/serovar (A/S) class. Isolates were serotyped by their co-agglutination reactions with a panel of 14 monoclonal antibodies (Boule Diagnostics, Huddinge, Sweden) using the nomenclature of Bygdeman.[5] Auxotyping was performed by standard methods.[4]

Results

The susceptibility patterns of the 56 strains to the antibiotics tested are shown in table 1. Twenty seven (48%) strains were penicillin resistant either through the production of penicillinase (PPNG) (10 isolates) or by chromosomal mechanisms (CMRNG) (17 isolates). There were 19 (34%) strains showing altered susceptibility to quinolones (QRNG). Five were in the less sensitive category and 14 were resistant to ciprofloxacin with the highest MIC, 4 mg/l, recorded for two strains. All isolates were susceptible to ceftriaxone and spectinomycin and none were TRNG. MICs to gentamicin ranged between 0.5 and 4 mg/l. Criteria for defining categories of gonococcal susceptibility to gentamicin are not well established but those available[6] suggest that 10 strains (18%) with an MIC of 4 mg/l were less sensitive.

The 56 gonococci were represented by 13 different A/S classes. Twenty four isolates were in the 1A and 32 in the 1B serogroup. Two A/S classes, Pro⁻/Arst (14 strains) and Nr/Bopt (19 strains), together accounted for 59% of all isolates. A further two A/S classes, Pro⁻/Arost and Pro⁻/Bopt, represented another 21% of the total so that 80% of strains were allocated to four of the 13 A/S classes. The remaining nine A/S classes contained between one and three isolates each.

The 10 PPNG were distributed among seven A/S classes. Three PPNG were Pro⁻/Arst and two Pro⁻/Arost. The 19 QRNG were distributed over eight A/S classes. Eight QRNG were Pro⁻/Arst, one with a ciprofloxacin MIC of 4 mg/l, five with an MIC of 1 mg/l, and two with an MIC of 0.12 mg/l. Four QRNG were Pro⁻/Bopt over a ciprofloxacin MIC range from 0.25 to 2 mg/l. Only one of the 19 Nr/Bopt A/S class was a QRNG.

Table 1 Minimal inhibitory concentrations (MICs) of the antibiotics (AB) penicillin (pen), ciprofloxacin (cipr), gentamicin (gent), ceftriaxone (ceft), spectinomycin (spec), and tetracycline (tetr) for 56 gonococcal isolates from Ulaanbaatar, Mongolia. MICs were determined by standard methods[3 4]

	MIC (mg/l)										
AB	⩽0.03	0.06	0.12	0.25	0.5	1	2	4	⩽8	⩽64	PPNG
pen		2	10	4	13	16	1				10
cipr	37		4	1		9	3	2			
gent					1	5	40	10			
ceft	56										
spec										56	
tetr									56		

PPNG = penicillinase producing *N gonorrhoeae*.

Discussion

The WHO recommends that any antibiotic treatment regimen should cure a minimum of 95% of cases treated. However, the antibiotic susceptibility of gonococcal isolates in Mongolia has been little studied. Results from this sample indicate the presence of significant resistance to the penicillins and quinolones. Resistance to the penicillins was by both chromosomal and plasmid mediated mechanisms.

Most of the isolates were concentrated among four A/S classes. However, both the PPNG and QRNG were phenotypically diverse. The large number of phenotypes and the wide range of MICs among the QRNG suggest that different mutations coding for quinolone resistance have arisen in many subtypes, rather than through spread of a single resistant "clone." This assumption would require verification by analysis of quinolone resistance determining regions of the chromosome. There were no PPNG and only a single QRNG in the commonest phenotype, Nr/Bopt.

All isolates tested were fully susceptible to spectinomycin and ceftriaxone. However, these antibiotics are not available in Mongolia, and for this reason the susceptibility of the strains to the aminoglycoside gentamicin, often used in this country to treat gonorrhoea, was examined. The correlation between in vitro susceptibility, as measured by MIC determinations, and clinical outcomes have not been firmly established for this antibiotic. One study in Malawi[6] suggested that strains with MICs of 16 and 32 mg/l should be regarded as resistant. All isolates tested here had MICs of 4 mg/l or less, probably indicating clinical susceptibility. The MIC methods used here and in the study of strains from Malawi differed, so that MIC values obtained in the two studies are not directly comparable. The E-test method was unreliable for estimating the susceptibility of gonococci to gentamicin.[6] Criteria for establishing resistance of gonococci to gentamicin by disc diffusion testing methods are yet to be established and would require the availability of gonococci with higher MICs than were

present in this sample. This development would assist in rapid screening of isolates for gentamicin resistance where this antibiotic is used.

The data suggest that a system for continuing appraisal of gonococcal susceptibility is needed in Mongolia to detect emergence and spread of antibiotic resistant gonococci and to guide selection of standard treatment regimens.

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Contributors: EL collected strains in Ulaanbaatar and examined them in Sydney; TRS and EAL assisted in susceptibility testing and phenotyping, database management, and isolate storage; EL and JWT analysed data; JWT wrote the text; and all revised the manuscript.

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